

Notice of Allowability

Application No.

10/763,953

Examiner

Jason M. Nolan, Ph.D.

Applicant(s)

KONG ET AL.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 03/26/2007.
2. ☒ The allowed claim(s) is/are 1,6-8,23,25 and 27 (now 1-7).
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date 03/28/2007
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☒ Interview Summary (PTO-413),
Paper No./Mail Date 4-2-07
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☒ Other PTLO-413B.

DETAILED ACTION

Claims 1, 2, 5-8, 23 & 25-27 are currently pending in the instant application; of which **Claims 1, 2, 5, 25 & 26** are currently amended and **Claim 27** is new.

Information Disclosure Statement

Applicants' information disclosure statement (IDS), filed on 03/28/2007 has been considered. Please refer to Applicants' copy of the 1449 submitted herein.

Response to Amendment

Applicant's amendments, see Amendment – After Non-Final Rejection, filed 10/12/2006, with respect to **Claims 1, 2, 5, 25 & 26** have been fully considered and are entered. The rejection of **Claims 25 & 26** has been withdrawn.

Rejoined Inventions

Claims 8, 23, 25 & 26 are directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(b), **Claims 1, 2, 5-7 & 27**, directed to the process of using the allowable product, previously withdrawn from consideration as a result of a restriction requirement, are hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Because a claimed invention previously withdrawn from consideration under 37 CFR 1.142 has been rejoined, the restriction requirement between **Groups I and Group II** as set forth in the Office action mailed on 10/14/2005 is hereby withdrawn. In

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view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Examiner's Amendment

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Danielle Herritt on April 2, 2007.

The application has been amended as follows:

1. In **Claim 1**, after "A method of treating" and before "comprising administering..." delete "a β -amyloid-related disease in a subject" and insert - - a disease selected from the group consisting of Alzheimer's disease, Down's syndrome, Mild Cognitive Impairment, age-related macular degeneration, and cerebral amyloid angiopathy in a subject in need thereof - -.
2. Delete/Cancel **Claims 2, 5 and 26**.
3. In **Claim 6**, after "The method according to" and before "wherein said..." delete "claim 2," and insert - - claim 1, - -.
4. In **Claim 7**, after "The method according to" and before "where said..." delete "claim 2," and insert - - claim 1, - -.
5. In **Claim 8**, before "selected from..." delete "A chemicalcompound" and insert - - A chemical compound - -.
6. In **Claim 25**, after "A pharmaceutical composition for the treatment of" and before "comprising a..." delete "a β -amyloid-related disease" and insert - - a disease selected from the group consisting of Alzheimer's disease, Down's syndrome, Mild Cognitive Impairment, age-related macular degeneration, and cerebral amyloid angiopathy - -.

Statement of Reasons for Allowance

The present invention pertains to the amidine derivatives in **Claim 8** and methods of using these compounds (or compositions) for the treatment of a β -amyloid-related disease in a human subject. Said compounds are free of the prior art; nothing known in the art anticipates or renders the compounds of the instant application obvious. The closest prior art related to these compounds has been made of record (see Non-Final Rejection, 04/27/2006). The β -amyloid-related diseases in which the compounds are effective for include Alzheimer's disease, Down's syndrome, Mild Cognitive Impairment, age-related macular degeneration, and cerebral amyloid angiopathy.

One skilled in the art would be enabled to make and use the compounds taught herein for the purpose of treating said diseases using the teachings of the specification in conjunction with the teachings in the prior art. Shown on pages 58-72 of the specification are the soluble A β assays, which give data on the ability of compounds to bind to an amyloid protein.

A recent review by Citron, M. (*Nature Reviews Neuroscience* **2004**, 5, 677-685) highlights the state of the art in strategies for modification in Alzheimer's disease. Stated therein: Alzheimer's disease (AD) affects more than 12 million individuals worldwide, and death occurs, on average, within nine years of diagnosis. The current standard of care for mild to moderate AD includes treatment with acetylcholinesterase inhibitors, and an NMDA antagonist has recently been approved for the treatment of advanced AD in the US. Two main disease mechanism-based approaches, which have

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been studied for more than 10 years, are based on the involvement of two proteins, amyloid- β ($A\beta$) and tau, in AD pathology. $A\beta$ is the main constituent of senile plaques, one of the key pathological characteristics of AD. Genetic and pathological evidence strongly supports the amyloid cascade hypothesis of AD, which states that amyloid- β 42 ($A\beta$ 42), a proteolytic derivative of the large transmembrane protein amyloid precursor protein, has an early and vital role in all cases of AD. The most direct approach in anti-amyloid therapy is the reduction of $A\beta$ 42 production.

The link between amyloid plaque and other diseases such as Down's syndrome have been established in, for example, the publications by Tanzi, R.E. (*Nature Medicine* **1996**, 2(1), 31-32) and Masters *et al.* (*Proc. Natl. Acad. Sci. USA* **1985**, 82, 4245-4249).

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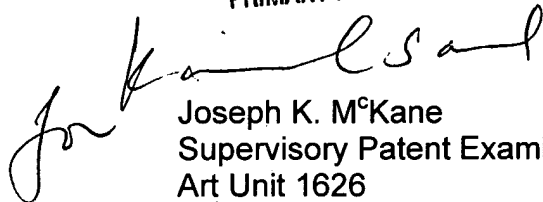
Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jason M. Nolan, Ph.D.** whose telephone number is **(571) 272-4356** and electronic mail is **Jason.Nolan@uspto.gov**. The examiner can normally be reached on Mon - Fri (9:00 - 5:30PM). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph M^cKane** can be reached on **(571) 272-0699**. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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Date: April 12, 2007